REMARKS/ARGUMENTS

With this amendment, claims 1, 15-17, 20, 24-25, 28-31 and 33-34 are pending. Claims 2-14, 19, 21-23, 26-27, and 32 are cancelled. For convenience, the Examiner's rejections are addressed in the order presented in an October 12, 2006, Office Action.

Applicants thank Examiners Ton and Singh for taking time to conduct a telephonic interview with Applicants' representative Beth Kelly on October 25, 2007. The rejection for alleged lack of enablement was discussed, as were possible claim amendments. Tentative agreement was reached and is reflected in the claims and arguments submitted in this response.

I. Status of the claims

Claim 1 is amended to recite treatment of an HIV strain that enters an immune cell using the CCR5 receptor. Claim 1 is also amended to recite that the beneficial gene is a polymorphism in the CCR5 gene having an encoded product that does not facilitate entry of an HIV virus into an immune cell. Support for these amendments is found throughout the specification, for example, at paragraph 41. Claims 1 is also amended to recite a homozygous polymorphism in the CCR5 gene. Support for this amendment is found throughout the specification, for example, at paragraphs 59 and 61. These amendments add no new matter.

II. Rejections for alleged obviousness-type double patenting

Claims 1, 15-18, 20, 24-25 and 27-34 are provisionally rejected for alleged obviousness type double patenting over claims 1-35 of co-pending US Application No. 10/498,450. Applicants will file terminal disclaimers to overcome these rejections, if appropriate, when the claims are deemed otherwise allowable.

III. Rejections under 35 U.S.C. §112, first paragraph, written description

Claim 1 and dependent claims 15-18, 20, 24-25, and 27-34 are rejected as failing to comply with the written description requirement. The Office Action alleges that the amended

claims include new matter by using the phrase "caused by a macrophage tropic stain of HIV in a human. . . " Office Action at page 4. In order to expedite prosecution, claim 1 is amended to recite treatment of an HIV strain that enters an immune cell using the CCR5 receptor. Claim 1 is also amended to recite that the beneficial gene is a polymorphism in the CCR5 gene having an encoded product that does not facilitate entry of an HIV virus into an immune cell. Support for these amendments is found throughout the specification, for example, at paragraph 41, which reads

> In one embodiment of this invention, the beneficial gene renders immune cells resistant to HIV infection. This gene can be **a polymorphism of a gene encoding any receptor that facilitates entry of HIV into the immune cells**. Receptors that mediate HIV entry include the primary cellular receptor CD4, as well as coreceptors, including, but not limited to, CXCR4, CCR5, CCR2b, CCR3, and CCR1. Suitable polymorphisms include those that interfere with expression of the receptor at the cell surface (*e.g.*, CCR5 delta 32, CCR5m303); ones that produce a receptor that is expressed, but unable to facilitate entry of the HIV virus (*e.g.,* CCR2-64I); and promoter polymorphisms that regulate coreceptor expression levels. . . . *Emphasis added.*

In view of the above amendments and remarks, withdrawal of the rejections for alleged addition of new matter is respectfully requested..

IV. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1, 15-18, 24-25, and 27-34 are rejected under 35 U.S.C. §112, first paragraph because allegedly, the specification does not provide enablement for one of skill to make and use an invention commensurate in scope with those claims. The Office Action also alleges that undue experimentation is required to practice the claimed invention. To the extent the rejection applies to the claims as amended, Applicants respectfully traverse the rejection.

In order to establish a prima facie case of lack of enablement, the Examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner has not provided any reason why those of skill would not be able to practice the claimed methods based

on the disclosure of the specification and on information that was publicly available at the time of filing.

The Office Action in large part alleges that undue experimentation is required to practice the invention. As set forth in the Manual of Patent Examining Procedure (MPEP) §2164.01, "the test of enablement is not whether any experimentation is necessary, but whether… it is undue." Further, the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

At page 10, the Office action asserts as a first issue that polymorphism of the CCR5 gene are not uniformly represented in the human population and that methods to expand the stem cells are allegedly unpredictable. Applicants request that the Examiner refer to the sentence spanning pages 13 and 14 of the October 12, 2006 Office Action, which, referring to a declaration and evidence submitted with the previous response states, "The declaration by Drs. Chow and Petz is persuasive in part; rejections pertaining to expansion of cord blood cell consistent with the declaration are withdrawn." Applicants resubmit below the arguments from the previous response, which based on the Office Action at pages 13 and 14, are sufficient to overcome the rejection. Applicants respectfully request that the Examiner refer to the previous response to view the originally submitted declaration and evidence.

> As described above, expansion of a population of stem cells before transplantation is not required to practice the claimed invention and the Office Action does not present any reasoning to suggest otherwise. Moreover, the specification at Examples 1 and 2 on page 13, provides the first disclosure of screening multiple cord blood samples to identify a source of stem cells that has a beneficial gene. Applicants present as

> Exhibit C, WO/2003/045335, a related PCT publication that discloses actual reduction to practice of the collection of stem cell sources from multiple unrelated cord blood donors. At paragraph 78, WO/2003/045335 discloses results of screening about five thousand umbilical cord samples from unrelated donors. Twenty two samples with homozygous CCR5 delta 32 polymorphisms were identified and about 500 samples with heterozygous CCR5 delta 32 polymorphisms were identified. Thus, Applicants are the first to demonstrate that sources of stem cells with beneficial genes, *e.g.*, umbilical cord blood, can be identified and collected for use in the claimed methods. This demonstration also provides evidence that allegedly unpredictable *ex vivo* or *in vitro* methods to expand stem cell populations are not required to practice the claimed invention. Thus, the specification teaches how to obtain a stem cell-rich population of cells for transplantation, *e.g.*, umbilical cord blood cells, and how to transplant the cells into a patient. Therefore, the claimed methods are enabled.
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> From response originally filed on July 17, 2006.

As a second issue the Office Action cites references that allegedly disclose that certain M-tropic HIV strains use receptors other than CCR5 to enter cells and that these disclosures demonstrate that the claimed methods cannot be predictably practiced by those of skill. The claims are now amended to recite treatment of an HIV strain that enters an immune cell using a CCR5 receptor. The claims are also amended to recite treatment only. Applicants believe that this amendment overcomes the rejections based on use of the phrase "M-tropic HIV strain."

As a third issue, the Office Action alleges that the specification does not disclose a number of stem cells that are required to be transplanted and elicit a protective immune response. This rejection also appears to be based on the alleged unpredictability of treating an M-tropic HIV strain by transplanting stem cells that express a mutation in a nuclei acid that encodes the CCR5 co-receptor. The Office action also alleges that the number of stem cells transplanted will be solely dependent on "severity of infection and usage of alternate co-receptor." Office Action at page 14. Applicants have amended the claims to recite treatment of

an HIV strain that enters an immune cell using a CCR5 receptor. Thus, the rejection for use of "M-tropic HIV strain" is no longer valid and should be withdrawn. The declaration with the previous response outlined the methods for transplantation of umbilical cord blood and replacement of the immune system in a human. According to the declarants, the particular disease treated by hematopoietic transplantation does not determine the dosage of stem cells used for treatment. Rather, the deciding factor is the size (weight) of the recipient patient. The Office Action does not provide any reasoning to indicate that those of skill are unable to determine patient weight and number of nucleated cells and/or CD34+ cells in a source of hematopoietic stem cells, *e.g.*, umbilical cord blood, without using undue experimentation. Therefore, the method of transplanting stem cell-rich populations of cells, *e.g.*, umbilical cord blood cells, into a patient infected with HIV or for prophylactic treatment of HIV is enabled.

In view of the above amendments and remarks, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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